ON THE RELATION OF THE ORGANIC PHOSPHORUS CONTENT OF VARIOUS DIETS TO DISEASES OF NUTRITION, PARTICULARLY BERI-BERI

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PART I.

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In November, 1910, Professor Ross called our attention to Fraser and Stanton's work on The Etiology of Beri-beri (1910), and asked us to enquire into the subject with a view to further researches on similar lines and at the same time supplied us with a large sample of a rice, the use of which as a diet had been associated with an outbreak of Beri-beri.

Shortly after we had commenced our work the monograph of Schaumann (1910) appeared in the Archives for Ship- and Tropical-Hygiene, and this work was found to be so complete and exhaustive that further investigation of the main facts seemed superfluous, and we turned our attention to confirming some of the newer facts and to further investigations of points—mainly of a chemical nature—arising out of his results.

Schaumann's work is so important that it seems advisable to give here an abstract of the more important sections of his monograph, which should be consulted for full details and also for the exhaustive bibliography.

After a historical review of the previous theories of the causation of Beri-beri and of the work of himself and others refuting these conceptions—e.g., a specific infection, contamination from without

by toxic bodies, or by autogenous development of such bodies in the diet, etc., he proceeds to the consideration of the work which connects 'Tropical Beri-beri' with the use of highly prepared rice—e.g., rice in which the husk and outer layers of the grain have been removed by the process of milling—and of that which connects 'Ship Beri-beri' with the use of similar rice as the staple diet, or with the use of preserved foods and other restricted or unsuitable diets.

Braddon (1909) first called attention, in 1901, to the fact that Beri-beri was prevalent in those Eastern tribes and races, e.g., Chinese, who used a highly-milled rice as their staple diet, but did not occur among races such as the Tamils, who cured their rice in such a way that the pericarp was not removed from the grain in the process of milling; Fletcher (1907) confirmed these observations, showing that the substitution of whole rice for polished rice in the dietary of the inmates of an asylum abolished Beri-beri, while the subsequent reversing of the diet led to an outbreak of the disease. Since 1907 polished rice has been abolished finally from the dietary of the inmates and Beri-beri has ceased, though previously extremely prevalent and causing many deaths. Fraser (1909) obtained similar results with gangs of labourers inhabiting separate compounds, and others have added further confirmation. The practical application of these observations by hygienists in our Eastern Possessions, in the Japanese navy and army, etc., has resulted in a great diminution of the incidence of the disease.

Turning now to another side of the question, Schaumann refers to the experimental production of polyneuritis in fowls; Eijkman (1897), in Batavia in 1896, discovered that fowls fed entirely on any variety of polished rice became lame and ultimately died, and demonstrated lesions in the peripheral nerves and anterior horn cells of the dead animals. On whole rice, however, no such symptoms were developed, and addition of the polishings to the prepared rice prevented their onset.

He further proved a similar difference between barley and prepared barley, and finally discovered that rice, barley and rye are no longer adequate after heating for a time to a temperature of 120° C., and birds fed on the above fall ill and die with typical appearances of peripheral neuritis. For diets so treated the name 'denaturised' is used.

Grijns (1908), in Batavia and Holland, confirmed Eijkman's results, and showed the development of polyneuritis in fowls when polished rice, sago and tapioca formed the sole diet, and that the same train of symptoms arose on a diet of flesh which had been heated to 120° C.

He discovered that the addition of small quantities of 'Katjang-idjo' beans (*Phaseolus radiatus* L.) rendered safe a diet previously injurious, and these beans also lost their preventive power if heated to 120° and *further demonstrated that the power of a rice to produce Beri-beri varied directly with the degree of preparation, that is with the extent to which the pericarp (or silver skin) was removed in milling.*

Axel Holst and Frölich (1907), working at Christiania with special reference to Ship Beri-beri and to scurvy, carried out a series of researches on pigeons and guinea-pigs, using various limited diets. Their results in the main confirm those of Eijkman and Grijns, both for prepared rice and barley and for heated foodstuffs. They demonstrated, in addition to the polyneuritis, marked emaciation in the birds and animals used, and also oedema of the subcutaneous tissues and muscles; further in mammals they found changes in the gums accompanied by loosening of the teeth.

In addition they examined various sorts of bread, and found that wheat bread was harmful both to pigeons and to guinea-pigs—bread baked with yeast, however, was much less harmful than bread baked with baking-powder. It should be noted that guinea-pigs are much less resistant than fowls to such restricted diets and that restriction of these animals to one sort of grain, whether ground or not, is invariably deleterious; rarefaction of the bones, haemorrhages in the neighbourhood of the epiphysial line, degenerations of bone marrow, and sponginess of the gums are often produced.

Holst further determined the amounts of peas, unshelled barley, etc., which required to be added to diets in order to prevent the onset of symptoms, and also calls attention to the fact that preserved meat has often been denaturised by heating to 120°.

Fraser and Stanton (1910) further confirmed these observations with regard to the association of polished rice and polyneuritis.

Schaumann (1908) and Fraser and Stanton (1909) (independently) discovered that diets which produced peripheral neuritis

were invariably poor in phosphorus, and that substances (e.g., rice meal, Katjang-idjo), which have the power of preventing the development of neuritis, are, on the contrary, rich in that substance; *indeed that the smaller the percentage of a diet in phosphorus the greater is its influence in producing Beri-beri in man, or neuritis in fowls.*

Schaumann thought that the active principle containing phosphorus was probably nucleic acid, and Grijns, following up this hypothesis, experimented with the nucleo-proteins of Katjang-idjo; no curative effect was observed with nucleins extracted by alkali, but some slight postponement of death was observed in neuritic birds treated with the phosphorus-containing extract obtained with hot water.

Schaumann further gives exhaustive tables of the composition of various food stuffs—grains (fresh and prepared), peas, beans, potatoes, meat, etc., both in the fresh and dried states, showing their composition with reference to protein, carbohydrate and fat, and in particular their various phosphorus-containing compounds—inorganic, phytin-like compounds, nucleins and phosphatides—and discusses the present state of our knowledge of the metabolism of these bodies.

Schaumann next proceeds to a critical review of the various theories of the etiology and points out that neither place, climate, nor season appear to be of importance, and that no specific organism has been isolated though many bacteriologists, and even Koch himself, have made careful investigations; Fletcher and Fraser also carefully excluded the question of infection since they showed that whether Beri-beri was present or absent among the inmates of a building or compound it could be banished by feeding with partly milled rice or called forth by feeding on wholly milled rice.

Braddon, with respect to Beri-beri, and Eijkman, with reference to Polyneuritis in birds, at first assumed that some toxic agent was present in the kernel of the grain which gave rise to Beri-beri and that the antidote to this toxin was present in the pericarp, and that so no bad effect followed feeding with the whole grain; but, if the pericarp were removed, the toxin already present or elaborated during digestion was free to exercise its effects. Others assumed that the fully shelled rice became contaminated more easily by toxic bodies (e.g., arsenic) and so caused ill effects, but Fraser and Stanton showed

that polished rice was equally deleterious when freshly ground as when it had long been exposed to the risk of contamination.

In spite of careful chemical investigations it has proved impossible to isolate any toxic body from polished rice, from denaturised (heated to 120°) flesh, or from other substances which cause Beri-beri or Polyneuritis; Fraser and Stanton further showed that sera, flesh, and other products of neuritic fowls caused no deleterious symptoms when administered orally or by injection to sound animals.

Schaumann then considers the theories which ascribe the development of Beri-beri to a faulty nutrition, and he calls attention to the theories of Nocht (1908); the latter ascribes both the multiform manifestations of Tropical Beri-beri and the usually milder Ship Beri-beri (which appears to be somewhat allied to scurvy), to dietetic errors; and lays special stress on the fact that it is not a question of defect of the main components of food stuffs—proteid carbohydrate and fat—but of some subtle defect of the less known constituents—enzymes, complements, compound proteids, etc.

Schaumann himself, however, is inclined to consider the substance or substances of importance to be organic compounds of phosphorus. He resolved first of all to investigate the possibility of the neuritis being due (1) to the development of oxalic acid by fermentation or to acidosis from deficiency of alkaline salts in the grain; (2) to the removal of ferments or other thermolabile substances by milling or 'denaturisation,' and (3) to investigation of the influence of phosphorus compounds, organic and inorganic.

He points out that the exact chemical nature of the phosphorus compounds in food stuffs and the body is but imperfectly known, that the methods of separation are but approximate and uncertain in many cases, and that the isolated products are probably modified by the processes of extraction, and so differ in physiological effect from their precursors.

Subject to modifications necessitated by the light gained in the process, he resolved to try diets, as polished rice and denaturised foods, which were known to produce neuritis, etc., and see whether any favourable results are obtained by the administration of such diets, with the addition of:—

1. Known organic and inorganic compounds of phosphorus.
2. Small amounts of substances rich in phosphorus, e.g., rice

meal, yeast, Katjang-idjo, wheat meal, testicular extract, or extracts from roe, etc.

3. Phosphorus compounds isolated by him from articles of food, e.g., yeast, Katjang-idjo, etc.

Special stress was attached to investigations with denaturised foods in which the defect was probably simpler than in milled foods, and Schaumann also planned to investigate microscopically and chemically the nerves and other tissues of the animals experimented on, and to carry out chemical investigations on fresh and preserved foods—foods from Beri-beri ships (and moulds, etc., contaminating them)—and also on the phosphorus excretion in faeces and urine of birds and Beri-beri cases.

Schaumann's first results show that excess of oxalic acid (or other toxic products) and deficiency in autolytic enzymes can play no part in the etiology of Beri-beri nor of Polyneuritis in fowls, and further that the fault of diet lies neither in deficiency of proteins nor of inorganic salts, since addition of these substances to a diet which gives rise to Polyneuritis has no protective influence, and also since the diets which Fletcher, Fraser and Ellis found to cause Beri-beri contain respectively 92, 103 and 99 grams of protein per man per day, a figure quite sufficient to maintain equilibrium, especially considering that Fletcher and Ellis were dealing with inmates of institutions for mental disorders and not with men engaged in hard manual labour. Turning now to phosphorus compounds, Schaumann gives exhaustive details of the various organic and inorganic compounds present in foodstuffs, and in the various organs of the body with their characteristics and the methods of extraction, etc. He then passes to a consideration of phosphorus metabolism; an adult man at work requires about two grams of phosphorus daily on mixed diet, while a dog seems to require less than 0·5 gram per day; birds in some instances require much larger amounts than mammals of the same size.

Passing on, he considers the metabolism of each of the better known classes of organic phosphorus compounds, phosphatides, nucleoproteins, phytin, etc., and also inorganic phosphates, giving an account of their absorption, assimilation, retention and excretion.

He calls attention to the fact that phosphorus is present in especially large amounts in the organs whose functions are most

complicated and important; further, the main organic phosphorus compounds are in large part assimilated by the alimentary tract as organic compounds, without the previous splitting off of the phosphoric acid, and the organs of man and the higher animals have further a marked power of storing excess of such compounds and of drawing on this store at times when these are deficient in the diet. He quotes Miescher's well-known work on the increase of salmon roe at the expense of the phosphorus of its muscles, and suggests that pregnant females may store up phosphorus to be subsequently given out in the milk. In addition to this, new-born animals usually possess a store of phosphorus proportionate to the length of time which will pass before they can forage for themselves (as is known to be the case also with iron). In times of hunger the animal organism is more economical of its phosphorus than of any other inorganic constituent, and seems to have a more urgent need of its phosphorus than even of its proteids.

Albu and Neuberg (1906) consider that it has been practically demonstrated that the body has not the power to synthesise the organic phosphorus compounds necessary for the life of the cells from phosphorus-free proteins and inorganic phosphates, *but that animal life is dependent for these substances (as for proteins and carbohydrates) on the synthetic powers of the vegetable kingdom.*

Schaumann next resolves to attempt as far as possible experimentally to determine the way in which an absence or deficiency of each or all of these compounds in the diet influences the animals, as Liebig has worked out the influence of salts on the growth of plants. The problem is much more difficult in the animal kingdom, however, since the substances are of great complexity, present great variety in each class, and are not only difficult to isolate but undergo important modifications in the processes of separation. These difficulties may lead to failure or to the results obtained experimentally being wrongly interpreted.

All earlier observers of neuritis, etc., in animals had considered that the causation of the lesion was to be attributed to some poisons (toxin, oxalic or other acid), which developed endogenously or exogenously in the nutriments producing them, and which could be neutralised by certain (equally hypothetical) anti-bodies which are present in certain food-stuffs, e.g., rice meal, *Phaseolus radiatus*,

etc. Fraser and Stanton (1909) have called attention to a parallelism between the lack of phosphorus in the food and the onset of Beri-beri in men and of neuritis in cattle, and in that have followed the suggestion made by Schaumann in 1908.

Schaumann's earlier experiments were not strictly conclusive as showing that lack of organically combined phosphorus was the most important and indeed the only factor in the etiology of Beri-beri, and his further experiments are planned with a view to attempting to find such conclusive proof.

Researches on Pigeons. Polished rice (20 grams per bird per day) forms, in the majority of cases, the basis of the food. It is used in the form of a pap or porridge, to which various amounts of the different substances can be added, with a view to determining their protective power; in other cases barley or barley bread was used as a basis, but these experiments have to be viewed independently of the rice experiments if the average time required for the development of neuritis, etc., is to be taken as a measure of the possession or lack of protective power.

Well-grown and well-nourished pigeons are found to be the most suitable for experiment, young animals and fancy breeds being less serviceable. Birds are specially suitable because their metabolism is very regular, and deficiency in the food is rapidly indicated. Further, the curative influence of protecting substances on sick birds is much more rapidly noticeable than on mammals.

Control experiments with pigeons showed that death occurred in the average period of thirty-five days on polished rice or rice bread; the birds exhibiting more or less severe appearances of lameness and losing 41 per cent. of their original weight.

If the rice is previously thoroughly extracted with cold water, the birds die much faster, in an average period of twelve days; extraction removed only 3·43 per cent. of the original proteid but 36 per cent. of the original phosphate; a difference of proteid per bird per day which would be unlikely to so hasten the end.

Non-protective Substances. Addition of dried egg-albumen, of albumen metaphosphate, calcium glycero-phosphate, and of inorganic salts (with or without phosphates), had no marked influence in either direction, as will be seen from Table I.

Nucleic acid from yeast prepared for commercial purposes

(scientific and medicinal) appeared to have a very unfavourable influence, but a specially manufactured sodium nucleate, carefully prepared to break up the molecule but little, seemed to have a slightly favourable influence. The birds only lived a few days longer than on rice alone, certainly, but the lameness was not marked.

Protective Substances. The meal or bran from the outer parts of grain which is removed in milling, however, had a very different influence when added to the polished rice pap used for feeding.

With two grams of rice meal (P_2O_5 3·8 per cent.) added to the pap for the day's ration, the birds remained fit and strong (for seventy-two days), and indeed gained in weight—1·5 gram per bird per day scarcely sufficed to keep them strong, and with 1 gram loss of weight commenced.

Equally favourable was the influence of the addition of wheaten bran, which contains 1·1 per cent. of P_2O_5. Four birds each received 2·5 grams of this per day, with the usual ration of rice pap. They lost some 20 per cent. of their weight, though otherwise remaining well for twenty-eight days; the ration was raised to 5 grams each per day, but as the birds did not recover their initial weight it was raised fourteen days later to 7·5 grams, and the birds in the next twenty-five days not only reached their original weight, but actually added a further 10 per cent., and were perfectly fit and active.

In a further set of five pigeons, two grams per bird per day of dried brewer's yeast (P_2O_5 4·2 per cent.) was added to the diet of rice pap; the birds remained well, but in two months lost a little (3·5 per cent.) of their weight. The allowance of yeast was reduced to one gram per bird daily, and except for the loss of a further 3·5 per cent. of their weight, they were at the end of a month apparently just as well as at the beginning of the experiment three months earlier.

Schaumann now compares these three 'protecting' substances as regards the phosphorus and proteid contents of the daily allowance needed to keep a pigeon well and maintain its weight, and it will be noticed that the phosphorus contents almost coincide.

Substance	Daily allowance (gram)	P_2O_5 content (gram)	Protein content (gram)
Yeast	1·5	0·063	0·55
Wheat bran ...	5·0	0·055	0·72
Rice meal ...	1·5	0·057	0·16

Curative Effects. In addition to trying the protective influence of these various substances when added to the polished rice diet from the beginning of the experiments, Schaumann also tried their power of curing pigeons which were already suffering from neuritis and in many cases were apparently very near to death.

In strange contrast to the fact that it exercised no protective power when administered in the diet from the beginning, is the effect of nucleic acid prepared from yeast when administered to birds already lamed by neuritis. Of fourteen cases in which this was administered (forced feeding), six died before the nucleic acid had passed out of the crop; in five cases with repeated forced feeding with nucleic acid and rice, some improvement manifested itself, but was only transitory, and the birds died in five days—the lameness which at first lessened having again returned.

In the remaining three cases the result was even better; rice pap containing 3·5 per cent. of yeast nuclein and of dry egg-albumen was repeatedly administered to one bird, which had lost 25 per cent. of its weight and was very lame and unable to move after fifty days' feeding on rice meal with egg-albumen; the next day the bird was able to walk with considerable agility, to use its wings in normal fashion, and to feed itself, and had lost the continuous convulsive movements of head and limbs that had previously troubled it. Twenty-four hours' further treatment, and the bird was apparently fully recovered and able to walk and even fly. Six days later it was killed and no degenerated nerve fibres could be found.

Similar results were obtained in the case of a second bird, which was not killed, however, and so no examination of the nerves was possible. The third bird apparently completely recovered on a similar treatment, and was able to fly on the third day of treatment. It was killed, and the usual appearances were found after death—oedema of the muscles of the limbs, other muscles with diffuse haemorrhages, numerous nerve fibres with typical appearances of degeneration in the sciatic nerve. In the upper limb nerves no degenerated fibres were found, however, and the general condition of nutrition appeared good.

Dried pressed yeast is even more powerful a curative agent than yeast nuclein. Unless the bird dies before the yeast has passed from the crop, its administration results invariably in recovery if a sufficient amount be given.

Schaumann has tried this in a large number of birds, small amounts (0·1 to 0·3 gram) have no effect, but one gram a day is quite sufficient. In birds not severely lamed, and able to feed themselves, recovery is fairly rapid. On addition of yeast to the diet, the symptoms of lameness disappear in a day or two, the weight regains rapidly its level on mixed diet, and the degenerated nerve fibres progressively diminish in number and in the amount of degeneration. (Only a few typically degenerated fibres were found in a bird killed on the sixth day, and after fourteen days no degenerated fibres were found, but a few still show 'foam-structure,' the earliest stage of degeneration, the last of regeneration.)

Schaumann takes for illustration in his text one of these birds, which had lost 40 per cent. (120 grams) of its weight on an exclusive diet of polished rice and was so severely lamed as to be on the point of death; 3 grams of dried rice pap with 1 gram of yeast was forcibly administered (the dried yeast contains 4·25 per cent. P_2O_5). The bird could walk fairly well in twenty-four hours, and after a further administration of 1 gram of yeast with its rice, was again able to fly. Schaumann gives photographs of this bird taken on these three days, and the improvement is most marked, especially as this bird had (also the first one mentioned as cured with yeast nuclein, photographs of which are also reproduced) convulsive movements of the head and limbs, accompanied by spasm of limbs and neck muscles (leading to retraction of the head), a condition which is of even more immediately fatal import than a severe degree of lameness.

After these two days the bird was able to feed itself, and received rice pap with addition of 5 per cent. of dried yeast. Its improvement was marked ('visible'), and in twelve days added 44 per cent. to its weight (80 grams).

Katjang-idjo beans (P_2O_5 1·08 per cent.) exert an excellent curative effect; lame birds are sufficiently restored in forty-eight hours to run and fly, and their weight rapidly increases—(30 per cent. in eleven days, 17 per cent. in four days). The amount of the bean required is about 1·3 gram per day for each bird.

Dry yellow peas were almost as effective as Katjang beans, curing five birds very rapidly.

Many organic phosphorus-containing extractives of plants and

tissues were also used for curative purposes. Nucleic acids from yeast have already been referred to and will be remembered to have some power.

Yeast lecithin appeared to have no curative influence, but seemed to have some protective effect, for one pigeon was still alive after eight weeks' feeding with rice pap to which 0·5 gram of yeast lecithin per day was added, and though it had lost some weight no lameness appeared.

Ovolecithin, tried in one case, improved the condition of the lamed bird at first, but the good effect was not permanent, and Katjang-idjo lecithin similarly seemed to have an initial but only transient curative effect.

Commercial phytin and protylin were tried and found to be valueless.

Schaumann separated several extracts from Katjang beans—the pepsin-hydrochloric acid extract contained a large proportion of the phosphorus and was a powerful curative agent. Administration of one gram per day for two days, followed by 0·5 gram for seven days, completely restored one markedly paretic pigeon; and a similar result was obtained with a body of the phytin group extracted from this bean, two lame birds being obviously better the day after its administration, but continuation of the treatment did not avail to completely restore the birds, or indeed to keep them alive.

Testicular extract has a distinct protective power; two birds to which 1·5 grams per day each was given with the rice pap lived respectively forty-eight and seventy-five days, on the average twice as long as on rice alone. Both showed great loss of weight (54 per cent.) and neuritis, though one was lame for a short time only, and the other lived for thirty days after symptoms of lameness had appeared. The same extract administered to a paretic bird improved its condition and materially delayed its death (probably by about thirteen days).

Schaumann here calls attention to the complete 'protective' and 'curative' influence of this extract in the case of dogs.

Some signs and symptoms are present in all the birds which are receiving polished rice alone or with non-protective additions. Diarrhoea with thin execretae is one of the most noticeable, the colour of the stools being decidedly green—the stools contain only about

25 per cent. of the phosphate present on a full mixed diet. Loss of body weight is also constant, varying in amount from 25 to 54 per cent. In nearly all cases the birds showed loss of appetite in the later stages, remained sitting and were unable to fly.

The differences in duration of life were very considerable, not only with different nutriments (non-protective), but even in the same series—the greatest variation in the same series was from twelve to sixty-one days.

Equally marked were the differences in the degree of incapacity which developed before death. In rare cases scarcely any weakness of the legs was observable even just before death occurred, and the birds might even fly shortly before the sudden onset of death. In other cases all grades of lameness of legs and wings may appear, some are quite unable to fly, and can only move with difficulty, walking uncertainly, stumbling and falling forward.

Irregularity and galloping of the heart beat occurs in a fair number of lame birds.

The same variability was shown in the degree of degeneration of the nerves of different birds of the same series when examined after death.

Schaumann states that the grade of lameness is no measure of the amount and grade of degeneration in the nerves; marked lameness with slight degeneration, or slight lameness with marked degeneration being both observed.

In one case no difference could be made out in the degree of degeneration of the two sciatic nerves of a pigeon, one excised when markedly lame, the other obtained by killing the bird when apparently fully restored by two days' feeding on Katjang beans. In other birds, which were killed after being apparently completely restored from their lameness by one or two feeds of curative material, the nerves were obviously very degenerated in spite of the fact that the paresis had completely disappeared.

Schaumann suggests that the phosphatic bodies may in some way serve as sources of energy (physical or chemical) in the nervous system, and refreshment of the supply enables the central nervous system to overcome the hindrance of the degenerated nerves.

The researches on pigeons have been given in some detail, and we propose to only briefly note those carried out on other animals.

Table I

Experiment	No. of birds	Nutriment	Additions		Neuritis	Average loss of weight per cent.	Average day of death
I	9	Pap from polished rice (20 gm. per bird per day)	—		—	41	35
II	3	Pap from extracted polished rice	—		—	26	12
III	3	Raw polished rice	—		—	44	33
IV	8	Polished rice pap	Dried egg-albumen		—	37	28
V	5	,,	Mixed inorganic salts without P_2O_5		—	39	32
VI	4	,,	Mixed organic salts Calcium biphosphate	1 per cent. 1·6 per cent.	Marked lameness appearing 4 to 11 days before death	35	27
VII	10*	,,	Albumen metaphosphate	1·6 to 33 per cent. (contains 7·8 per cent. P_2O_5)	Marked lameness	29	23
VIII	4	,,	Calcium glycero-phosphate	1·6 per cent.	,,	33	19
IX	4	,,	'Scientific' yeast nucleic acid	1 per cent. (P_2O_5 5·54 per cent.)	More or less severe lameness	36	27
X	5*	,,	'Medicinal' yeast nucleic acid	1 per cent. (P_2O_5 16·3 per cent.) and 1·6 per cent. egg-albumen)	All much lamed in 15 days	33*	15*
XI	2	,,	Sodium nucleate (yeast)	1·5 gm. per bird per day (8 per cent. P_2O_5)	Lameness not marked	50	39
XII	2	,,	Testicular extract, (Bull)	1·5 gm. per bird per day (3·5 per cent. P_2O_5)	Lameness came on slowly, and was not extremely marked till just before death	54	61

* Several of these birds were used for experimental cure. Average figures are taken from remainder.

Guinea-pigs kept on polished rice or maize, with or without the addition of yeast, die during the fourth week; the loss of weight is between 20 and 40 per cent., and though lameness is not noticeable there are signs of early degeneration in the nerves. In addition, haemorrhagic lymphadenitis may develop in animals on yeast. In many animals, also, rarefaction of bones (osteoporosis) was very evident, and the bones might be as thin as paper.

Rats were kept on a diet of egg-albumen, starch (potato), sugar and inorganic salts, with or without phosphate (albumen-metaphosphate); death occurred in about 40 days without apparent lameness; on fine rye bread, denaturised by heating with soda, they die in 63 days (average), losing 47 per cent. of their weight.

Rabbits.—Maize, and maize with egg-albumen, is inadequate: death occurs in 45 days, with slight degeneration, and the loss of weight is about 30 per cent; other symptoms are lameness and loss of reflexes in the hind limbs, loss of hair, loss of appetite and activity; they die of exhaustion or convulsions. One strong rabbit lived after ninety-seven days' feeding on rice and egg-albumen.

Maize with the addition of 4 per cent. of dried yeast is fully adequate and maintains the animals in normal health.

Katjang-idjo and peas rapidly restore animals which have become paretic—the lameness vanishing and the body weight rising rapidly.

An Ape, which thrives on rice pap, currant bread, nuts and fruit, died with paresis and loss of nearly 30 per cent. of its weight after seventy-four days' feeding on pap from polished rice previously extracted with water. There was little typical degeneration, but nearly all the nerve fibres showed 'foam-structure.'

In the next set of animals, *denaturised horse flesh* was used as the basis of diet. The flesh is heated in an autoclave to 120° C. with dilute soda-solution—the alkali being afterwards neutralised with hydrochloric acid. The nuclein molecule is probably split in the process. The proteids are not apparently affected. (Neither ammonia nor sulphur bases are formed.)

Rats, on denaturised flesh, become paretic in about a month, but the illness does not progress, and the experiments were abandoned after three months or more. Loss of weight, about 5 per cent.

Cats.—Denaturised flesh: death in about 50 days; loss of weight, 30 per cent. Lameness present before death; slight nerve changes demonstrated.

Dogs.—Denaturised flesh (about 1 kg. a day); loss of weight, 25 per cent; death, 50 days (average). Severe lameness starting in the hind limbs is the first symptom, and progresses to complete incapacity; death occurs with convulsions. In one case there was *sponginess and haemorrhages* in the mouth and gums, with ulceration; nerve degeneration is only slight. One dog lived for fifty-five days and was kept quite fit and well by the addition to the diet of four grams a day of testicular extract; in the earlier stages with larger amounts (six grams) of extract he put on additional weight to the extent of 11 per cent. (1,200 grams), showing that the horse flesh is not deficient in caloric value, but the testicular extract (P_2O_5 3·36 per cent.) supplies some essential substance. The testicular extract was replaced on the 56th day by 5 grams of yeast, with the result that the dog gained 1,150 grams (15 per cent.) in weight in thirty-one days and was very well and active.

Though dogs die in 50 days on the average on denaturised flesh, this one lived three months in full health, when some five grams a day of these substances (rich in phosphorus) were added. He was now kept on denaturised flesh alone, and in 50 days had lost 2,550 grams and was severely paralysed. Four days later, when death was apparently imminent (the pulse was 270), ten grams of fat-free yeast were administered—the dog improved and was able to move in twenty-four hours (pulse now 100). For three further days five grams of yeast were given and the dog had completely recovered and was visibly fatter.

Similar rapid cure was obtained in other cases with testicular extract—one animal gained a kilogram in six days after treatment was begun.

Schaumann emphasises the fact that the symptoms and changes in these animals are similar to those found in sailing ship Beri-beri, and that in patients with that disease, as in the animals, the reaction to a more suitable diet is exceedingly prompt.

Tropical Beri-beri differs more particularly in the length of time required for recovery, which is often many months.

By feeding a goat on rice and maize till lameness and loss of weight were marked, and repeatedly reviving it with Katjang beans and yeast, either in single doses or continued for short periods, Schaumann prolonged an experiment for six months. The goat

was at the end very weak and paralysed, and was slow in reacting to curative treatment. The animal was killed and extremely careful examinations made of its organs. Degenerative changes were present in the nerves and some wasting was also shown in the columns—no alteration of the cellular elements was demonstrable. Some alterations were detected in the vagi, and the muscles were oedematous and markedly rich in nuclei.

The appearances and symptoms were suggestive of those of Tropical Beri-beri.

Schaumann gives full details of his various experiments on animals, with an account of the results of the post mortem and microscopic findings and tables of averages. He also gives the results of exhausitve analyses of all the substances used for feeding in these experiments, with special references to the amounts and characteristics of the different classes of phosphorus compounds present in them, and to various extracts obtained by solvents (acids, alkalies, etc., peptic and pancreatic digestion).

He draws the following conclusions from his experiments on animals.

CONCLUSIONS

I. Food stuffs which lead to the development of Polyneuritis in animals are characterised by a low content of phosphorus or of certain organic compounds of phosphorus. This may be either fundamental or be caused by artificial processes.

II. Animals are not protected from the ill effects caused by such diets by the addition thereto of proteids, inorganic salts, inorganic phosphates, or the synthetic organic compounds of phosphorus (calcium glycero-phosphate, albumen-metaphosphate).

III. The addition of certain substances, rich in organic phosphorus, to such diets exercises both a protective and a curative effect. Yeast, rice meal, wheat bran, peas, Katjang beans, and testicular extracts are the chief substances with this power. Carnivora and herbivora, however, react rather differently to testicular extract, the former are completely protected, the latter only in a less degree.

IV. Artificially separated organic phosphorus compounds of various kinds, prepared from these natural protective substances, exercise only a moderate and transient influence. Such compounds

include yeast nucleic acid, phytin-like compounds from Katjang, phytin from rice meal, and possibly certain phosphatides.

V. Apparently the protective or curative effect of these substances is dependent not on any one of their organic compounds of phosphorus, but on the collective effect of a number of these. Animals do not apparently possess the power of forming the organic phosphorus compounds necessary to their economy from inorganic phosphates by their own metabolism, but are dependent for their provision on the plant world, as they are for other classes of foodstuff (e.g., protein and carbohydrate).

VI. The metabolism of phosphorus and nitrogen stand in close relationship to one another.

VII. Spontaneous or experimental polyneuritis in animals appears to be a disease of metabolism, attributable to the lack of some specific organic phosphorus compounds whose identity is still uncertain.

SAILING SHIP BERI-BERI

Turning now to the subject of Ship Beri-beri, Schaumann points out that this disease generally occurs on sailing ships on the return voyage, that it does not usually attack the majority of the crews, and that change of diet, particularly fresh meat and vegetables, exercises a rapid and complete curative effect. (Crews are mainly Europeans.)

In his tables are given the logs of the voyages of ten sailing ships, the incidence of Beri-beri among their crews, the provender and its appearance, and the men's statements as to the cooking and palatableness of the various articles of diet. In a second set are analyses of the various foodstuffs from the ships and others of fresh foodstuffs for comparison; these show the alterations in proteid, etc., due to preservation and long storage, more especially with reference to their phosphorus contents; further examinations were made of the substances after cooking, again with special reference to the behaviour of their phosphorus and eatability; the moulds present were also examined. In other tables are given the results of analyses of the excretae of Beri-beri patients and the results of experiments on animals with the provender from the ships, etc.

He notes first that the phosphorus excretion of the patients is

exceedingly low (50 per cent. of normal), and that it rapidly rises on phosphorus rich diets but some retention of phosphorus occurs.

He points out that the various customary articles of diet carried on sailing ships fall into two groups: rice, white bread, and potatoes, etc., in the one group, poor in phosphorus, are known to give rise to neuritis in animals.

Of the other group of substances, rich in phosphorus, the salt meat has been shown to lose nearly 50 per cent. of its phosphorus by the combined action of the pickle lye and of the water used in boiling, König (1904). Schaumann's results confirm this loss in the meat from the Beri-beri ships, and further show the presence in the lye of purin bases, which must arise from breakdown of nucleo-proteids.

The peas and other legumes are found to be usually mouldy, are hard and resistant to cooking even with soda. They are frequently quite uneatable, and many Beri-beri patients turn against them, and Schaumann further shows that their phosphatides seem to have undergone considerable changes.

Preserved vegetables carried on one ship were very rich in organic phosphorus, and had been found to be extremely valuable in the treatment of the sailors stricken with Beri-beri. Preserved meat is also rich, particularly in lecithin phosphorus.*

Schaumann considers that the cause of Beri-beri on ships lies in the lack of organic phosphorus compounds in the diet of the sailors. This is especially noticeable on the return voyage (especially in ships loading home from nitrate and guano ports where fresh meat and vegetables are not obtainable), in part owing to the sailors being partly driven to bread, rice, etc, through the mouldiness of the peas or their hardness from keeping (rendering them impossible to soften even when boiled in soda), or the decay and smell of the meat. To this is added in other cases the loss of organic phosphorus in the salt meat due to the action of the lye, and the similar loss in the leguminous foods owing to standing or to boiling with soda.

He calls attention again to the affinity between scurvy and ship Beri-beri (*vide* also his animal experiments), and suggests that scurvy may be found to be due to use of stale vegetables, and Beri-beri to use of rotten or stale flesh—the important factor in each being lack of organic compounds of phosphorus.

* Schaumann does not appear to note that this article must often be denaturised by heating to 120° in preserving. (Holst, *loc. cit.*)

As a curative agent, he says all sailors know the value of fresh meat and vegetables. As a preventive agent, he suggests that it might be possible to carry dried yeast, rice meal or testicular extract for use when the ordinary diet becomes inadequate, and especially lays stress on the probable value of requiring all ships engaged on voyages where fresh provender may be difficult to obtain, to carry a supply of Katjang beans in sealed (sterilised) cases. In the future, he hopes a more active principle requiring but small bulk may be isolated.

Sailing ship Beri-beri is a disease of metabolism dependent on lack of organic phosphorus in the diet.

TROPICAL BERI-BERI

Schaumann's observations on this disease are in part based on the conclusions of workers in the East, and in part on clinical and therapeutic observations on patients in the Hospital at Hamburg. Tropical Beri-beri contrasts with sailing ship Beri-beri in being chiefly observed among the Chinese stokers, trimmers, etc., of steamships, who cook for themselves and keep to their accustomed dietary even when on board. The dietary is usually frugal, considering the hard work they perform.

Fletcher and others have shown that Tropical Beri-beri is connected with the long continued use of a predominating amount of polished rice in the diet (uncured rice is used synonymously with polished rice). Grijns and others have shown the same connection of polished rice with polyneuritis, and rice meal or its alcohol extract (Fraser and Stanton) prevents the occurrence. Breaudat (1910) has demonstrated that rice meal (the part removed in polishing) has a similar curative and prophylactic influence in Tropical Beri-beri.

Analyses of the total mixed diets of Fraser, Fletcher and Ellis show that they are quite ample in carbohydrate, proteid and fat, and in caloric value for the requirements of men, judging by ordinary physiological standards, and the development of Beri-beri cannot depend on lack of these substances. On the contrary, the diets containing polished rice and causing Beri-beri contain only about two-thirds of the phosphorus requirements (4·5 grams) of a man, even

if a high average value is taken as a basis of calculation, and must often be less than this figure. The process of cooking may further reduce this. The pericarp which forms the difference between Beri-beri rice and wholesome rice is specially rich in organic phosphorus and in fat, but contains no other peculiar substances as far as can be determined. Grijns showed that the fat is not the important principle, and so we are left only with the phosphorus compounds.

Schaumann gives analyses showing that the urinary excretion of phosphorus in patients with Beri-beri is much below the normal (average 50 per cent.), and this is accompanied by an almost equal diminution of urinary sulphur and nitrogen. Previous observers found even larger differences (70 per cent.). Addition to the diet of substances rich in phosphorus leads to a marked rise in the excretion of all these bodies.

Aron (1910), by careful experiments on the metabolism of a Beri-beri patient extending over four weeks, showed that he was unable to obtain sufficient phosphorus and nitrogen on the diet used before the attack to meet his requirements, which were higher than is normal. Remedy of the defects resulted in rapid cure. Aron further showed that outbreaks of Beri-beri on ships often occurred about six or eight weeks after the substitution for that previously used of a rice with a much lower phosphorus content—possibly only one-third of the previous, the rest of the diet remaining unaltered.

Hirota (1900) has shown that nursing children (in Japan) often develop severe Beri-beri two or three weeks before their mothers, and improve rapidly on change of milk. This is associated with a great diminution of the phosphorus (especially in organic combination) of the milk, and would seem to be associated with phosphorus hunger in the mother, resulting in a retention and sparing of phosphorus.

Hulshoff Pol (1910) has demonstrated that Katjang beans form, with regard to polyneuritis in animals, a *certain and rapid* cure for Beri-beri, and extract of the beans is equally efficacious. He further showed that addition of a similar amount (150 grams) to the dietary of various pavilions in an asylum absolutely abolished Beri-beri; vegetables were less effective. The staple diet in the asylum consisted of polished rice.

This has been confirmed by many others, and though the chronic lesions of Beri-beri usually disappear very slowly under treatment,

occasionally the paralysis disappears with the startling rapidity observed in the experiments on animals.

Schaumann and Werner tried the therapeutical effects of phosphorus-rich compounds on Tropical Beri-beri and obtained improvement by the use of yeast, nucleic acid, testicular extract, etc., though the improvement was not so marked as in polyneuritis in animals, owing to the more advanced lesions in these cases requiring longer for regeneration. (Fat-free yeast and carefully prepared nuclein should alone be used.) Katjang beans, peas, and also the peptic extract of Katjang are also very valuable.

On these grounds it appears clear that Tropical Beri-beri resembles experimental Polyneuritis and Ship Beri-beri in being due to lack of organic phosphorus in the diet, but *it appears to be due to a chronic deficiency of long duration, with severe deep-seated lesions requiring a long time to cure.* The experimental neuritis in a goat already described is analagous to Tropical Beri-beri. The other experimental cases and Ship Beri-beri, on the contrary, are due to a sudden large deficiency of organic phosphorus, and the lesions, though severe, are not deep-seated, and are rapidly recovered from.

In the majority of cases, *Beri-beri is due to a gross deficiency of the organic phosphorus in the diet.* In other cases the differences may be individual in the patient, since some individuals require much larger amounts than others, and others again may be unable to absorb and assimilate the compounds, though present in the diet. Schaumann quotes the case of a German colonist, who, after being very ill with malaria on the Amazon, developed Beri-beri on the voyage home though on an ample diet; in this case the intestinal absorption appeared faulty, as there was a great deficiency in urinary, and a very large increase in the faecal phosphorus.

Occasionally, epidemics of Beri-beri appear to be due to a bacterial infection of the gastro-intestinal tract, either through the catarrh interfering with absorption or to the bacteria (or their products) absorbing or splitting the organic phosphates before they could be absorbed.

Tropical Beri-beri is a disease of metabolism due to the amount of organic phosphorus compounds assimilated being below that essential for the human organism.

This is in the majority of cases due to deficiency of organic phos-

phates in the diet, but may in occasional cases be due:—(*a*) to deficient absorption of organic phosphates by the alimentary tract, or (*b*) to bacterial infection possibly splitting the phosphates before absorption or interfering with the absorptive power of the intestine.

CONCLUDING CONSIDERATIONS

A whole cycle of other diseases in all probability have a similar etiology to that of Beri-beri, more especially Ship Beri-beri. Scurvy has already been conclusively shown to be of this nature by a whole series of observations, and to all appearance Infantile Scurvy, Rickets, and Osteomalachia are also included. Pellagra and the form of malnutrition described by Czerny and Kellner in artificially fed children may be further examples.

The suspicion arises that all these diseases may be due to deficient assimilation of organic phosphorus, but it is difficult to understand how a similar cause can produce the different effects shown by the symptoms in these diseases.

It has already been shown that the animal organism is not adapted to build up organic phosphorus compounds for itself, but depends for these on the plant kingdom, and it is probably equally unable to form compounds of one group from those of another (e.g., nucleo-proteids from phosphatides).

Since different groups play different rôles in the economy of man, it is certain that deficiency of each group will have its own special effect, and in addition this will be complicated by an associated influence on the general metabolism; for example, inorganic compounds would react on the alkaline earths of the bones, nucleo-proteids would react on the proteins, etc.

Individual differences would further intervene to complicate the picture, more especially age differences, and infancy, childhood, puberty, pregnancy and old age would, in particular, have a far-reaching influence.

So by deficiency of single groups, or of combinations of groups of phosphorus compounds, various symptom complexes—different diseases—may be originated. Thus lack of nucleo-proteid in adults is probably connected with Beri-beri; in children a similar deficiency might give a different disease: deficiency of phosphatides may give yet a third, a combination of the two will give yet another picture.

Application of the principles already applied to Beri-beri in this paper may bear fruit also in these diseases, though only after long and complicated researches may the answers be obtained.

Schaumann hopes that his speculations may lead to encouraging further researches along systematic lines. While quite recognising that they are but hypotheses resting on slight grounds, yet the advance of science and medicine would be but slow were it not largely aided by experimenters, who have striven with all the means in their power to prove or disprove theories based on even slighter grounds; and Schaumann has felt it right not to conceal his speculations, as they may yet bear fruit.

We feel that this monograph is so thorough and complete, and so well thought out, as to deserve communication at considerable length, especially as recent occurrences have shown us that it, like the previous researches of other workers on similar lines, has not become as widely known in physiological, scientific and medical circles in this country as it would had it not been published in a journal mainly concerned with Tropical medicine. We think that all readers will agree with us that Dr. Schaumann is to be congratulated, not only on his important contribution to our knowledge, but on its arrangement and its literary merit.

To our nation, with its wide shipping interests and tropical possessions, it is the more important, and we must congratulate ourselves that it is largely based on the work of British medical men and scientists in our Eastern possessions. Their work has already had widespread influence in checking the heavy incidence and mortality of Beri-beri.

In 1910, Fraser and Stanton published a further paper carrying on their work on these lines, and have further confirmed the association of organic compounds of phosphorus with the deficiency of diet causing Beri-beri.

Our own researches as far as they have extended are in full agreement with those of Schaumann, though results have as yet only been obtained with our experiments on pigeons.

We can confirm the unfavourable influence of polished rice, steamed rice, and steamed barley fully; and the protective influence of whole rice, whole barley, rice meal, yeast and Katjang-idjo. The curative effects of yeast in pigeons severely affected with

neuritis were even more marked than we had expected, and we were astonished at the rapidity and completeness with which the birds recovered.

It was not our intention to communicate any of our results till considerably more experiments and analyses had been concluded, nor indeed to abstract previous work at such length as we have done.

The great public attention, however, which has been directed for some months to the question of our bread, led us to call attention to this literature in a letter to the British Medical Journal of May 6th, and now to communicate in detail those of our results which bear on this problem. We had so many enquiries for references that we thought it right to quote the previous work at some length, since the problem of the influence of rice in Beri-beri is so closely allied to that of a standard bread.

It is interesting to remember that the Germans refer to Rickets as the English disease, and to reflect that it is far more common in this country than it is in Germany, and further that the Highlanders and our Irish peasants are in large measure free from it.

Yet the children of all these races are brought up largely on similar diets (excepting such as are bottle-fed from the start). In the poorer classes of all, milk forms some part of the diet; in the peasant class it is usually good, in the town children it is often, however, neither abundant nor containing cream. Besides this, the children get their main nutriment from the national bread and from rice. Polished rice is used in all the nations, but the Highland child gets porridge from oats, the Irish child potatoes, the German rye bread, and the English child white wheat bread.

The organic phosphates are undoubtedly present in the oatmeal (0·9 per cent. P_2O_5) of the Highlander, and in the potatoes (unless deeply peeled); in the rye bread the organic phosphorus appears to be diffused through the whole grain (P_2O_5 1 per cent.), and even fine rye bread does not originate polyneuritis in fowls (Holst) or in rats (Schaumann).

In the fine English white wheat bread, however, the phosphorus has been removed with the bran, and is used largely (as is rice meal) as one of the best possible foods for fattening cattle. White wheat bread (P_2O_5 0·2), as Holst has shown, causes polyneuritis in fowls and Schaumann shows the existence of the important protective phosphates in the wheat bran.

Our own researches fully confirm Holst's results; indeed, the effects were more markedly deleterious than he found. The bread was a white flour bread, guaranteed to be made from the finest white flour, unbleached and unadulterated. Well nourished pigeons when limited to this bread devoured it greedily, but failed to flourish. Diarrhoea, and loss of weight, early commenced; listlessness and lameness followed shortly after. The first bird died on the 15th day, and others on the 16th and 20th days, showing marked degenerative changes in their peripheral nerves. Several were revived when extremely weak and nearly ready to die, showing severe lameness and, in some cases, the convulsions and retraction of the head described by Schaumann; but the average duration of life (allowing one or two days for the revived birds) was 29 days, and the average loss of weight 26 per cent.

Far different is the picture on Standard or whole-meal bread. The birds continue active and well, maintain their weight, clean and plume themselves; they remain able to fly and walk, and at the end of seven weeks were all perfectly well and had, on the average, gained 8 per cent. of their original weight. On whole-meal bread in two cases, pairing occurred; one pair successfully hatching the two eggs (though the diet was changed to a mixed diet during the sitting); the other pair were put on white bread, broke the eggs and began to go downhill.

These results are given more completely in the tables at the end of this article, and appear to us, in conjunction with Holst's, Leonard Hill's (B.M.J., April 30), and Schaumann's, to fully confirm the claims of the advocates of Standard or whole-meal bread.

We have seen that some degree of rickets is almost universal among the children of our poorer classes, who, in addition to lack of sunlight and fresh air, live largely on white wheat bread, and that it is not so prevalent in those nations whose children eat porridge (oatmeal 1 per cent. P_2O_5), or rye bread, with a higher content of organic phosphorus compounds. We know that they often get little else but poor milk and *margarine* (P_2O_5 0·03 per cent.), which may also be deficient in similar compounds, and we see that marasmus, diarrhoea, oedema of the limbs, spasm and convulsions (especially tetany) are common to rickets and to the experimental neuritis of pigeons and animals.

It seems to us that Schaumann's hypotheses are not likely to long

lack justification with regard to this disease and also to its close ally, infantile scurvy, though the symptom complex is probably complicated by secondary effects on digestion and on the metabolism of lime and proteid.

It may be objected that our white bread is baked with yeast and so the missing organic phosphates are compensated for, but the amount of yeast used is very small and probably insufficient (Holst's pigeons died on yeast bread towards the end of three months; more slowly, it is true, than on bread baked with baking powder (average 40 days), but none the less surely). And it must further be remembered, that much of the bread now sold is made with baking powder and not with yeast, and so a further factor making for deficiency is introduced. Failures of absorption, bacterial infections, and other internal disorders no doubt play their part as in Tropical Beri-beri, but it may well be that success of the present agitation for a wholemeal bread will have a wide reaching effect on the betterment of the physique of our nation, in lowering our death rate and in lighten ing the overcrowding of our hospitals.

The following tables include the results of experiments referred to in the text. Some of the series are merely confirmatory of the results of previous observers; others refer to the experiments with white and Standard bread. The results of curative treatment with yeast and other substances are also briefly alluded to, and in a final table the results of analyses (E. S. E.) of various substances used are given.

We hope in a future contribution to give the results of our attempt to isolate the active principle, whether it be one of the organic phosphorus compounds or a substance which associates itself with these in its reactions, as do ferments with nucleo-proteids. We wish at the present time to express our indebtedness to Professor Sherrington, Professor Moore, Miss Tozer, and others for their kindness in advising and assisting us in various chemical and neurological problems that have confronted us.

In conclusion, we wish to emphasise the great importance of these investigations to a country such as this with wide Shipping and Colonial interests, and hope that an appreciation of these facts will lead to the adoption of the necessary additions, where such diets are largely used, as has already been done in the Straits Settlements with striking results.

TABLE II

Series	No. of Pigeons used	Nourishment	Average weights in grams					Percentage difference of weight		Average day of		Remarks
			1st day	8th day	15th day	22nd day	End	—	+	Marked incapacity	Death	
A	6	Uncleaned rice (Paddy)	342	364	375	369	373	...	9	...	...	Expt. abandoned 56th day, all quite healthy
B	6	Polished rice (known to have caused Beri-beri)	329	284	236	236	201	39	...	32	34	
D	6	Polished rice (from a Liverpool shop) ...	316	268	226	200	180	43	...	32	35	
l	3	Uncleaned rice (denaturised at 120° C)	350	312	276	251	251	28	...	19	22*	*See protocol
m	3	Denaturised rice + 2 grams dried yeast per bird daily	369	377	335	374	374	...	1	...	...	Expt. abandoned 35th day, all quite healthy
n	3	Denaturised rice + 2 grams denaturised yeast daily	324	295	259	224	206	36	...	22	25*	
E	6	Barley grain	334	344	352	367	364	...	9	...	...	Expt. abandoned 30th day, all quite healthy
F	6	Barley grain (denaturised at 120° C.) ...	367	378	343	289	198	46	...	33	37	
C	6	Polished rice + mineral phosphates ...	350	346	298	275	256	27	...	36	38	
a	5	Standard bread (yeast 0·3 per cent.) ...	372	375	381	378	384	...	3	...	...	Expt. abandoned 50th day, all healthy
d	6	Wholemeal bread (yeast 0·3 per cent.)...	328	306	365	340	330	...	3	...	...	Expt. abandoned 36th day, all healthy
b	5	White bread (yeast 0·3 per cent.) ...	348	324	283	258	245	30	...	27	32	
c	6	White bread (yeast 0·3 per cent.) ...	347	349	306	276	...	21	...	18	20	

TABLE III.—Successful Restoration Experiments

Series	No.	Previous diet	Percentage loss of weight	Day of treatment	Type of neuritis	Treatment	RESULTS
C	2	Polished rice	31	40 *et seq.*	Peripheral	Yeast	Improved 24 hours. Flying 48 hours.
C	4	Polished rice	29	34 ,,	Vestibular	Yeast	Improved 24 hours. Flying 48 hours.
D	1	Polished rice	39	29 ,,	Vestibular	Maize and Soya oil	Improved 3 days. Weight regained, 14 per cent. in 3 weeks
D	3	Polished rice	25	29 ,,	Vestibular	Maize and Soya oil	Improved 3 days. Weight regained, 20 per cent. in 3 weeks
F	2	Steamed barley	39	28-31 day	Vestibular	Yeast (3 days)	*Full recovery 3 days.* Relapsed later, on omission of yeast
l	1	Steamed rice	24	16 *et seq.*	Vestibular	Yeast	Improved rapidly. Flying 3 days
l	2	Steamed rice	36	19 ,,	Vestibular	Yeast	Improved 24 hours. Flying 48 hours
l	3	Steamed rice	24	28 ,,	Slight peripheral	Yeast	Improved 2 days. Weight regained, 13 per cent. in 2 weeks
n	2	Steamed rice : steamed yeast	24	27 ,,	Peripheral	Yeast	Improved rapidly. Flying 48 hours
n	3	Steamed rice : steamed yeast	32	25 ,,	Vestibular	Yeast	Improved rapidly. Flying in 3 days
b	2	White bread	36	43 ,,	Peripheral	Katjang	Improved 24 hours. Weight regained, 19 per cent. in 7 days
c	1	White bread	25	21 ,,	Peripheral	Yeast	Regained 17 per cent. weight in 7 days
c	3	White bread	18	20 ,,	Peripheral	Yeast	Regained weight competely in 2 weeks
c	4	White bread	16	23 ,,	Vestibular	Yeast	Flying in 3 days. Weight regained, 15 per cent. in 7 days
P	2	Rice and lecithin	29	21 ,,	Peripheral + Vestibular	Standard bread	Improved slowly. Lameness continued for 7 days
Q	1	Rice and nuclein	32	20 ,,	Vestibular	Standard Bread	Improved rapidly. Feeding in 24 hours. Weight regained, 19 per cent. in 7 days
Q	3	Rice and nuclein	33	23 ,,	Vestibular	Standard bread	Improved rapidly. Feeding in 24 hours. Weight regained, 18 per cent. in 7 days
b	1	White bread	28	49 ,,	Peripheral + Vestibular	Yeast	Flying, walking, and feeding in 24 hours

degeneration could be discovered in small cutaneous nerves, in the anterior and posterior spinal roots, in the vagi, or in the vestibular nerves in spite of careful search in several cases. Nor did any degeneration appear to be present in the spinal cords.

Series l and F

The rice and barley grain used in experiments A and E was also used in these series, but was previously exposed to a temperature of 120° C. for two hours in an autoclave.

The birds on steamed rice failed very rapidly, marked convulsive neuritis occurring on the 16th and 19th days respectively, and the birds would certainly have died in the course of forty-eight hours. Forced feeding with ordinary brewers' yeast (and rice) was instituted, and in both instances the birds were free from convulsions and able to walk in twenty-four hours, and in a further day appeared quite normal.

Professor Sherrington kindly examined one of these birds for us before and after the first twenty-four hours of yeast feeding. Before treatment started it could barely stand and held the head completely retracted; on attempting to walk it became convulsed and turned a series of back somersaults till brought up by some obstruction; the wing reflex (flap reflex) was absent, and the eye and head reflexes were abnormal. The next day it could walk and fly readily, the wing reflex and head reflexes were normal, and all signs of labyrinthine trouble had disappeared. The third bird became very weak on the 24th day, and was barely able to move or feed itself. It rapidly recovered on yeast feeding and change of diet. In Table I, in reckoning the probable day of death, an ample margin has been allowed.

The birds on denaturised barley failed slightly less rapidly, the first died with convulsive seizures on the 22nd day, the last on the 45th day. One was restored on the 28th day when very near death by yeast feeding, which was continued for three days. It failed again on the barley diet and died on the 44th day.

Series m

Shows the absolute adequacy of a diet of denaturised rice, with the addition of one gram dried yeast per bird per day.

SERIES n

Shows that the protective influence of the yeast is entirely destroyed by heating to 120° C. The birds showed typical neuritis and other symptoms usually associated. Two rapidly recovered on treatment with ordinary yeast.

PERCENTAGE OF P_2O_5 IN VARIOUS DIETS USED :—

		Percentage of P_2O_5
Polished rice	6 samples	0·26
Rice meal	4 ,, ...	2·75
Uncleaned rice	3 ,, ...	0·61
Dried yeast	4 ,, ...	4·03
Katjang beans	2 ,, ...	0·95
Barley grain	3 ,, ...	0·92

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